

PACKAGE LEAFLET

Package leaflet: information for the user

AmBisome®
Liposomal Amphotericin B 50 mg
Powder for Concentrate for dispersion for infusion

Read all of this leaflet carefully before you start using this medicine.

Keep this leaflet. You may need to read it again.

If you have any further questions, ask your doctor.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

In this leaflet:

1. What AmBisome is and what it is used for
2. Before you are given AmBisome
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1. What AmBisome is and what it is used for

What AmBisome is

AmBisome is an antifungal antibiotic. The active ingredient in AmBisome is amphotericin B.

AmBisome is given as an infusion into a vein (a drip) by a doctor or nurse.

What AmBisome is used for

AmBisome has been studied in patients aged one month and above.

AmBisome is used to treat serious infections caused by fungi:

- **Fungal infections of one or more organs inside the body**
- **Suspected fungal infections** in patients who have a **raised temperature and a low white blood cell count called *neutropenia*.**
Before you are given AmBisome your doctor will check that your fever is not due to bacteria or viruses and will try and treat the infection with a course of antibiotics.
- **Visceral leishmaniasis**, a disease caused by a parasite.

AmBisome is not used to treat common fungal infections that are not serious, for example skin infections

2. Before you are given AmBisome

Before your first treatment

Before your first treatment your doctor may give you a small amount of AmBisome. They will then wait for approximately 30 minutes to see whether you have an allergic reaction, before continuing the infusion of the full dose.

Your doctor will not give you AmBisome:

- **If you are allergic** (hypersensitive) to amphotericin B or any other ingredients of this medicine (listed in section 6). However, if **your condition is life-threatening** you may be given AmBisome if your doctor believes that only AmBisome can help you.
- **If you have previously had a severe allergic reaction** (*anaphylactic* or *anaphylactoid*) to AmBisome. Symptoms of such immediate and life-threatening allergic reactions include: flushing, itching, sickness, swelling of the face, mouth, tongue and airways, often enough to cause difficulty breathing.
→ **Tell your doctor** if any of these applies to you, **you must not be given AmBisome**

Your doctor will take special care with AmBisome:

- **If you have a severe allergic** (*anaphylactic* or *anaphylactoid*) **reaction**. If this happens your doctor will stop the infusion.
- **If you get other reactions related to the infusion**. If this happens, your doctor may slow down the infusion, so you receive AmBisome over a longer period of time (approximately 2 hours). Your doctor may also give you medicines to prevent or treat infusion-related reactions, such as diphenhydramine (an antihistamine), paracetamol, pethidine (for pain relief) and/or hydrocortisone (an anti-inflammatory medicine that works by reducing the response of your immune system).
- **If you are taking other medicines that may cause kidney damage**, see the section *Other medicines and AmBisome*. AmBisome may cause damage to the kidney. Your doctor or nurse will take regular blood samples to measure your *creatinine* (a chemical in the blood that reflects kidney function), and electrolyte levels (particularly potassium and magnesium) because both of these can be abnormal if you have changes in your kidney function. This is particularly important if you are taking other medicines that can affect the way your kidney functions. The blood samples will also be tested for changes in your liver, and your body's ability to produce new blood cells and platelets. **If blood tests show a change in kidney function**, or other important changes your doctor may give you a lower dose of AmBisome or stop treatment.
- **If blood tests show that your potassium levels are low**. If this happens, your doctor may prescribe a potassium supplement for you to take while you are treated with AmBisome.
- **If you are receiving or recently had a white blood cell transfusion**. Sudden and severe problems in the lungs can happen if you are given AmBisome infusion during or shortly after a white blood cell transfusion. Your doctor will recommend that the infusions are separated by as long a period as possible. This will reduce the risk of lung problems, and your lungs will be monitored.
- **If you have kidney failure and are having dialysis**. Your doctor may start AmBisome treatment after the procedure has ended.

- **If you have diabetes.** AmBisome contains approximately 900 mg of sucrose (sugar) in each vial. Tell your doctor if you have diabetes.

Other medicines and AmBisome

Tell your doctor if you are taking any other medicines, or have recently taken any. This includes medicines and herbal products you bought without a prescription.

Medicines that may cause kidney damage:

- **Medicines that suppress the immune system** (*immunosuppressants*), such as ciclosporin.
- **Certain antibiotics** called *aminoglycosides* (including gentamicin, neomycin and streptomycin).
- **Pentamidine** a medicine used to treat pneumonia in people with AIDS and leishmaniasis.

➔ **Tell your doctor if you are taking any of these medicines.** AmBisome may make any kidney damage caused by the medicine worse. If you are taking any of these medicines, your doctor or nurse will take regular blood samples to check your kidneys.

Medicines that may lower your potassium levels:

- **Corticosteroids**, anti-inflammation medicines that work by reducing the response of your immune system.
- **Corticotropin** (ACTH), used to control the amount of corticosteroid produced by your body. The body produces corticosteroid in response to stress.
- **Diuretics**, medicines that increase the amount of urine your body produces. This includes furosemide.
- **Digitalis glycosides**, medicines produced from the foxglove plant and used to treat heart failure. AmBisome may worsen the side effects of digitalis, such as heart rhythm changes.
- **Muscle relaxants** usually used during surgery, such as tubocurarine. AmBisome may increase the muscle relaxant effect.

➔ **Tell your doctor if you are taking any of these medicines** or have had recent surgery where these drugs may have been used.

Other medicines:

- **Antifungal medicines**, such as flucytosine. AmBisome may worsen the side effects of flucytosine. This includes changes in the body's ability to produce new blood cells. This may be seen in blood tests.
- **Certain cancer medicines**, such as methotrexate, doxorubicin, carmustine and cyclophosphamide. Taking this type of medicine with AmBisome may cause kidney damage, wheezing or trouble breathing and low blood pressure.
- **White blood cell transfusions.** Sudden and severe problems in the lungs can happen if you are given AmBisome infusion during or shortly after a white blood cell transfusion. Your doctor will recommend that the infusions are separated by as long a period as possible. This will reduce the risk of lung problems and your lungs will be monitored.

➔ **Tell your doctor if you are taking any of these medicines** or receiving such transfusions.

Pregnancy and breast-feeding

Tell your doctor before you are given AmBisome if you are pregnant, planning to become pregnant, or if you are breast-feeding. Your doctor will only prescribe

AmBisome if they think the benefits of treatment outweigh the risks to you and your unborn child or your baby.

Do not drive or use machinery

Some of the possible side effects of AmBisome could affect your ability to drive or use machines safely, See Section 4, *Possible side effects*.

AmBisome contains sugar

Tell your doctor if you have an intolerance to sucrose or other sugars

Tell your doctor if you have diabetes. AmBisome contains approximately 900 mg of sugar (sucrose) in each vial.

Important information about some of the ingredients of AmBisome

AmBisome contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially 'sodium-free'.

AmBisome contains soya oil. If you are allergic to peanut or soya, do not use this medicinal product.

3. How AmBisome is used

AmBisome is always given to you by a doctor or nurse. It is given as an infusion into a vein (a drip).

AmBisome must not be given by any other method.

To prepare the infusion AmBisome must be dissolved in sterile water for injection and then diluted with a solution containing dextrose. AmBisome must not be mixed with saline (salt) solutions or with other drugs or electrolytes.

AmBisome is not interchangeable with other amphotericin products.

Before your first treatment

Before your first treatment your doctor may give you a small amount of AmBisome. They will then wait for approximately 30 minutes to see whether you have an allergic reaction, before continuing the infusion of the full dose.

Dosage for adults and the elderly

Your dose of AmBisome will depend on your body weight and your own particular needs.

- **Fungal infections of one or more organs of the body:**

Treatment is normally started at 1 mg per kg of body weight, every day over 3 to 4 weeks. Your doctor may decide to increase the amount you receive to as high as 3 mg per kg body weight.

- **Suspected fungal infections in patients with a raised temperature and neutropenia:**

Treatment is normally started at 1 mg per kg body weight, per day. Your doctor may

decide to increase the amount you receive to as high as 3 mg per kg body weight.

- **Visceral leishmaniasis:**

The usual dose is 1 to 1.5 mg per kg body weight, per day for 21 days, or 3 mg per kg body weight for 10 days.

If you have a severely weakened immune system (for instance, if you are HIV positive), the dose is 1 to 1.5 mg per kg body weight for 21 days. Due to the risk of re-infection, on-going treatment or a further course of treatment may be needed.

Dosage for children

AmBisome has been used to treat children. The dose of AmBisome for a child is calculated per kg of body weight in the same way as for adults.

AmBisome is not recommended in babies under 1 month old.

Dosage for patients with kidney problems

No change in dose or frequency of infusion is required. Your doctor or nurse will take regular blood samples to test for changes in kidney function during AmBisome treatment.

How long will the infusion take?

Normally the infusion will take 30 to 60 minutes. For doses greater than 5 mg per kg of body weight per day, the infusion could take up to 2 hours.

4. Possible side effects

Like all medicines, AmBisome can cause side effects, although not everybody gets them.

Tell your doctor immediately if you have a severe allergic reaction, chest pain, develop an irregular heart beat or kidney problems (signs include tiredness and passing less urine). Severe allergic reaction side effects may include: skin rash, difficulty breathing, wheezing, chest tightness, swelling of the airways/tongue/face/hands or feet, loss of consciousness, confusion or dizziness, rapid or irregular heart beat, vomiting and nausea.

Side effects during the infusion

You may get side effects during the infusion:

- **Very common** (*may affect more than 1 in 10 people treated*): fever, chills, and shivering.
- **Less frequent infusion-related side effects include:** chest tightness, chest pain, breathlessness, difficulty breathing (possibly with wheezing), flushing, a faster heart rate than normal, low blood pressure and musculoskeletal pain (described as joint pain, back pain, or bone pain).

These side effects clear up quickly when the infusion is stopped. These reactions may not happen with future infusions of AmBisome or with a slower infusion (over 2 hours). Your doctor may give you other medicines to prevent infusion-related reactions, or to treat the symptoms if you do get them. If you have a severe infusion-related reaction, your doctor will stop the AmBisome infusion and you should not

receive this treatment in the future.

Very common side effects

(may affect more than 1 in 10 people treated)

- Low blood potassium levels, leading to feeling tired, confused, having muscle weakness or cramps
- Feeling sick or being sick
- Fever, chills or shivering.

Common side effects

(may affect up to 1 in 10 people treated)

- Low magnesium, calcium or sodium blood levels, leading to feeling tired, confused, muscle weakness or cramps
- High blood sugar levels
- Headache
- A faster heart rate than normal
- Widening of the blood vessels, causing low blood pressure and flushing
- Breathlessness
- Diarrhoea
- Stomach pain
- Rash
- Chest pain
- Back pain
- Abnormal results for liver or kidney function showing up in blood tests or urine tests.

Uncommon side effects

(may affect up to 1 in every 100 people treated)

- Bleeding into the skin, unusual bruising and bleeding for a long time after injury
- Fits or seizures (*convulsions*)
- Difficulty breathing, possibly with wheezing
- Pain and swelling around the vein where AmBisome has been infused.

Other side effects

It is not yet clear how frequently these side effects occur:

- low red blood cell levels (*anaemia*), with symptoms of excessive tiredness, being out of breath after light activity, and a pale complexion
- Heart attacks
- Kidney failure
- Severe swelling of the skin around the lips, eyes or tongue
- Breakdown of muscle
- Bone pain and joint pain

Interference with Phosphorus blood test results.

This medicine may interfere with a particular blood test that measures levels of phosphorus (called the PHOSm assay). Please tell your doctor that you are receiving this medicine before such blood tests.

➔ If you notice any side effects that you are worried about, whether they are listed in this leaflet or not, **tell your doctor.**

5. How to store AmBisome

AmBisome is stored in the pharmacy.

Keep out of the reach and sight of children.

Do not use AmBisome after the expiry date which is stated on the label.

Do not store above 25 °C. Do not store partially used vials for future patient use.

AmBisome is a single dose, unpreserved, sterile, freeze-dried yellow powder to be dissolved in water for injection and diluted with a dextrose solution before infusion into a vein. From a microbiological point of view, the product should be used immediately once dissolved and diluted. If it is not used immediately, in-use storage times and conditions prior to use are the responsibility of the doctor or pharmacist and would normally not be longer than 24 hours at 2°C to 8°C unless reconstitution (dissolving the powder in water for injection) and dilution have taken place in controlled conditions to prevent microbial contamination.

Where reconstitution (dissolving the powder in water for injection) and dilution with dextrose solution are carried out under controlled conditions the storage time varies depending on the concentration of dextrose used and the storage temperature. Please refer to the Summary of Product Characteristics for further information.

Do not use AmBisome if there is any evidence of deterioration or foreign matter.

6. Further information

What AmBisome contains

The active ingredient of AmBisome is amphotericin B. Each vial contains 50 mg of amphotericin B enclosed inside liposomes (small fat particles). The other ingredients are: hydrogenated soy phosphatidylcholine, cholesterol, distearoylphosphatidylglycerol, alpha tocopherol, sucrose (sugar), disodium succinate hexahydrate, sodium hydroxide and hydrochloric acid.

What AmBisome looks like and contents of the pack

AmBisome is a sterile, bright yellow Powder for Concentrate for Dispersion for infusion.

It is presented in a 15 ml, 20 ml or 30 ml glass vial.

Each vial contains 50 mg of the active ingredient amphotericin B.

The closure consists of a rubber stopper and an aluminium ring seal fitted with a removable plastic cap.

Each carton contains 10 vials and 10 filters.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Gilead Sciences International Ltd.
Cambridge
CB21 6GT
United Kingdom

Manufacturer:
Gilead Sciences Ireland UC
IDA Business & Technology Park
Carrigtohill
County Cork
Ireland

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder

This leaflet was last revised in MM/YYYY.

To report any side effect(s):

Please contact the relevant competent authority

THIS IS A MEDICAMENT

- Medicament is a product that affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions for the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.

Keep all medicaments out of reach of children.

Council of Arab Health Ministers and Union of Arab Pharmacists

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